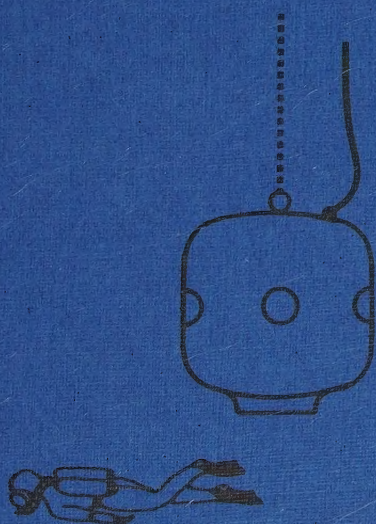


Ulf Balldin

DECOMPRESSION SICKNESS
AND NITROGEN ELIMINATION IN MAN:
INFLUENCE OF IMMERSION, BODY POSITION
AND AMBIENT TEMPERATURE
with special reference to hemodynamics



Lund 1973

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av

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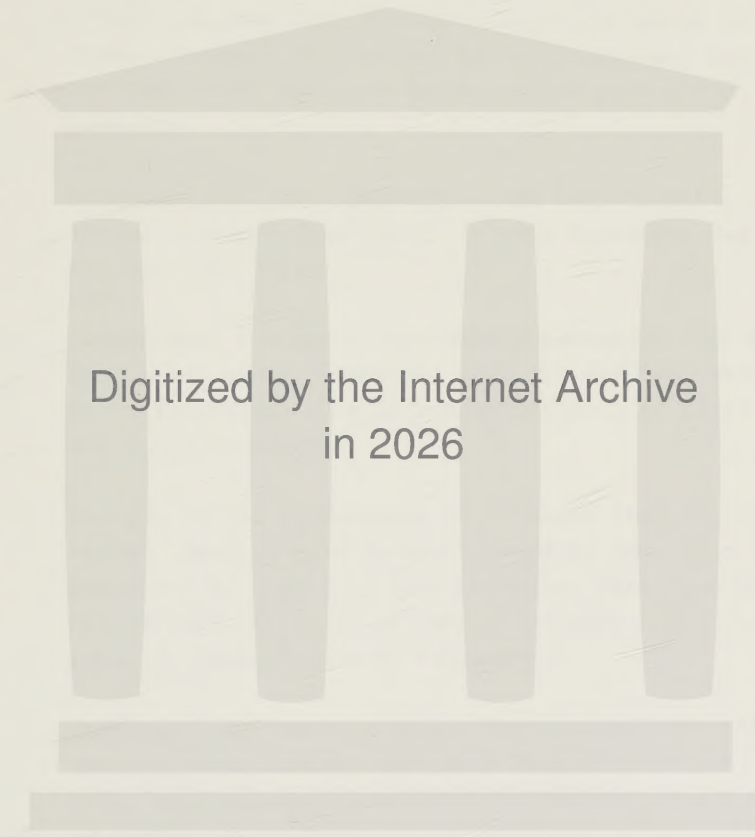
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This thesis is based on the following papers which in the text will be referred to by their Roman numerals:

- I. Effects of immersion with the head above water on tissue nitrogen elimination in man. Aerospace Med. 43: 1101-1108, 1972. In collaboration with C.E.G. Lundgren.
- II. Effects of ambient temperature and body position on tissue nitrogen elimination in man. Aerospace Med. 44: 365-370, 1973.
- III. Hemodynamic changes in man during immersion with the head above water. Aerospace Med. 43: 593-598, 1972. In collaboration with M. Arborelius Jr., B. Lilja and C.E.G. Lundgren.
- IV. Changes in the elimination of ¹³³Xenon from the anterior tibial muscle in man induced by immersion in water and by shifts in body position. Aerospace Med. 42: 489-493, 1971. In collaboration with C.E.G. Lundgren, J. Lundvall and S. Mellander.
- V. Regional lung function in man during immersion with the head above water. Aerospace Med. 43: 701-707, 1972. In collaboration with M. Arborelius Jr., B. Lilja and C.E.G. Lundgren.
- VI. The preventive effect of denitrogenation during warm water immersion on decompression sickness in man. Försvarsmedicin (Stockholm) 9 (3), 1973. In press.

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INTRODUCTION

When the human body is exposed to reduced environmental pressure, as occurs during flying and during the ascent from diving, inert gas that is kept in solution within the tissues may be liberated and cause decompression sickness. If this is to be avoided, the pressure reduction must be controlled at a rate which is slow enough to allow sufficient transport of the dissolved inert gas from the tissues to the lungs. This may preclude tissue gas pressures which are dangerously high relative to the ambient absolute pressure. Therefore much of the time during manned undersea activity is spent under very long lasting decompressions when a diver is returning from deep and prolonged dives. For instance, commonly used decompression tables prescribe that an air breathing diver who has worked for 90 min at 75 meters of depth spend 11 hr and 22 min on returning to surface pressure (18). Surfacing after a helium saturation dive at 300 meters requires the diver to remain in the decompression chamber for about 12 days (49). It is well known that presently used decompression tables do not completely preclude decompression sickness. Therefore, it is of great importance to seek methods which allow faster decompressions or improved safety. In a survey of proposals for accelerating inert gas elimination to reduce the duration of the decompression, Lambertsen (31) presents three main principles: increased partial pressure gradient of the inert gas, increased activity of dissolved gas molecules (for faster diffusion) and increased perfusion of tissue. The first two principles are based on the application of physical fundamentals. The most extensively applied method of physical character is to provide a breathing mixture with the highest possible oxygen pressure during decompression. Thereby a maximal inert gas pressure gradient is obtained between the tissues and the arterial blood. Unfortunately, the use of this method is severely limited by the

toxic effects of oxygen at high pressure on the central nervous system (5) and the lungs (14).

Physiological methods devised to increase inert gas elimination should aim at influencing blood circulation (cf 31). One of the first methods to be investigated was physical exercise (8). As reviewed by Jones the inert gas elimination in skeletal muscles during oxygen breathing increases during exercise as the perfusion of the muscles is increased (28). However, the circulatory adjustments to exercise may reduce inert gas elimination in some of the tissues. It is also known that exercise actually increases the incidence and intensifies the symptoms of decompression sickness probably because mechanical tension causes cavitation in the tissues (16,44).

The stimulating effect of mild hypoxia on blood circulation is reported to reduce slightly the frequency of symptoms associated with decompression sickness at altitude (48). Artificially induced hypoxia, however, does not seem to be a suitable method for use in practical decompressions.

Carbon dioxide admixture to inhaled oxygen may also enhance the nitrogen elimination, presumably via influences on tissue perfusion (36). The carbon dioxide seems to increase the nitrogen elimination mainly in tissues with fast nitrogen clearance rates, while in tissues with slow clearance there may be a decrease (36). Thus, the value of using carbon dioxide in the inhaled gas for reducing the risk of decompression sickness is a priori questionable. The incidence of decompression sickness was not influenced by increased carbon dioxide pressure in inhaled air as reported by Gray (23), but an increased risk of decompression sickness during hypercapnia was found by Hodes and Larrabee (24). Observations have also been made in this laboratory indicating that carbon dioxide accumulation might increase the severity of

decompression sickness once it occurs (4).

It has been theorized that hyperthermia may increase inert gas elimination via influence on tissue blood perfusion. Thus, Lambertsen predicted that intermittent over-warming will add to the safety and efficiency of decompression (31). It is noteworthy that Greek sponge divers use to treat victims of decompression sickness by packing them in hot sand (9), and hot baths have also been recommended apparently on an empirical basis as treatment for Russian divers (46). Furthermore, as pointed out by Lambertsen: "Long experience in open sea diving has confirmed that cold water and local or general lowering of body temperature predisposes an individual to development of bends" (31). Low environmental temperature also seems to increase the likeliness of altitude decompression sickness (16,40). This is probably because the vasoconstrictor response to cold interferes with inert gas exchange. However, the effects of temperature on inert gas exchange have apparently not been systematically investigated.

Theoretically, another way of increasing the rate of inert gas elimination would be to use drugs which promote the blood circulation. Unfortunately no suitable drug seems to be available yet which would not, while increasing blood flow in some tissues, decrease it in other tissues. Thus, the risk of dangerous gas liberation may rise in the latter tissues.

A survey of mechanisms influencing blood circulation and thus possibly inert gas exchange should take into account the effects of changes in body posture. Cardiac output is known to increase when changing from erect to supine position (10,35,50). This change is brought about by a redistribution of blood from dependent body regions to the pulmonary circulation and the heart. One might assume that similar

mechanisms are operant when the body is immersed in water. However, earlier measurements of cardiac output during immersion are conflicting and no reports are available concerning inert gas exchange during this procedure (cf III).

Purpose of the present study

The present work was designed to investigate if environmental factors in diving or compressed air work might modify inert gas elimination and thus the risk of decompression sickness. The study focused on the influence of immersion (I), body position (II) and ambient temperature (I and II) on nitrogen elimination in man. Indeed, these factors were found to influence nitrogen elimination and this influence was thought to be elicited by changes in the blood circulation. Therefore, the central (III) and peripheral (IV) hemodynamics were studied as well as the regional lung function (V) with regard to ventilation and perfusion during some of the different experimental conditions used in the nitrogen elimination studies. Finally, the practical applications of the findings were studied in a series of experiments on the influence of denitrogenation during warm water immersion on decompression sickness in man (VI).

Experiments involving invasive techniques and provocation of decompression sickness are not completely without risks. The risks have carefully been taken into consideration and the ethical aspects were attended to in consultations with several independent medical research workers.

CHAPTER I

THE INFLUENCE OF IMMERSION, BODY POSITION AND AMBIENT TEMPERATURE ON NITROGEN ELIMINATION

Immersion is likely to influence circulation mainly by counteracting the pooling of blood in dependent regions of the body caused by gravity. If the water level during immersion is above the heart level a negative intra-alveolar pressure is created relative to the immersed parts of the body. Such a negative pressure is known to reduce the functional residual capacity of the lungs (1,2). This reduction has partly been ascribed to intra-thoracic blood pooling. It was considered likely that this circulatory effect of immersion might influence cardiac output and peripheral blood flow and thus the nitrogen elimination. The maximal hydrostatic pressure difference between the outside of the chest wall and the alveolar air that a diver may be subjected to under normal conditions amounts to about 35 cm of water column (27). That is the mean depth difference in the upright position between the lungs and the mouth and it occurs when the breathing gas has the same pressure as the water at the mouth level. A pressure difference of approximately this magnitude was obtained in subjects sitting upright by immersing them to the neck.

The cardiac output is known to be greater in the supine than in the erect body position (cf Chapter II). This difference is brought about by shifts in blood distribution. It may be of practical significance because divers and compressed air workers are free to vary their body positions while in a pressure chamber. It was therefore decided to compare the rate of nitrogen elimination in the sitting and supine body position.

The circulatory effects of environmental temperature loads on the body will depend on the magnitude of these loads. How-

ever, when choosing the ambient temperatures for studying thermal influence on nitrogen elimination, the comfort of the subjects had to be considered. Furthermore, from the applied point of view moderate deviations from neutral temperature were considered most relevant. The temperature levels chosen for the immersion experiments were 32°C, 35°C and 37°C and for the non-immersion experiments 25°C, 28°C and 37°C for cool, neutral and warm temperatures, respectively (cf I and II).

METHODOLOGICAL CONSIDERATIONS

In the present studies (I and II) the expired nitrogen was collected during rebreathing in a closed spirometer system with a carbon dioxide absorber and a fan for mixing the gas. An adjustable inlet of very pure oxygen (99.995 %) served to maintain a fixed and low nitrogen concentration (1.72 %) throughout the experiments. A near maximal nitrogen pressure difference between alveolar air and tissues was thus maintained. The subjects, wearing swim trunks, were encased in a body container. In order to preclude nitrogen diffusion through the skin (cf 7,29) from the container, the latter was flushed with oxygen in both the non-immersion and immersion experiments. The temperature in the container was regulated with a heat-exchanger.

In prolonged nitrogen elimination studies using a closed spirometer system it is important that leakage of air into the system can be kept minimal. The inward leakage of nitrogen into the system was checked in conditions resembling the experimental situation as closely as possible. A continuous inward nitrogen leakage, never exceeding 7 ml/hr, was observed which probably occurred through the walls of the rubber tubes.

A conventional analysis of error taking into account the accuracy of the nitrogen meter, the volume recording system

and FRC calculations indicated a maximal error of the nitrogen volume determinations of ± 50 ml at the end of the experiment, the error in paired comparisons being considerably smaller.

Double determinations were made in each subject in all experimental situations. Each subject served as his own control which reduced the importance of factors which might cause individual differences in nitrogen elimination, such as body composition. Furthermore, physical activity before the experiments was limited and the diet was standardized to minimize nitrogen from alimentary sources. When reference is made to a subject's body weight as being normal, it complied with a standard for desirable body weights (51).

RESULTS

Immersion

Measurements of nitrogen elimination during immersion (wet conditions) were made in water at three different temperatures, 32°C , 35°C and 37°C . Under the present experimental conditions these water temperatures may be considered as cool, neutral and warm respectively, as corroborated by recordings of ear temperature, pulse rate and oxygen consumption (cf I). The control situation (non-immersion) in an environmental gas temperature of 28°C may also be considered thermally neutral (I).

The relative differences between eliminated nitrogen volumes during immersion and in control experiments (I) are summarized in the upper part of Fig 1. In all the 5 subjects ($n=10$, i.e. 10 paired dry and wet experiments) studied, a larger nitrogen volume was recovered during the first 30 min of immersion, irrespective of water temperature than during the same period of time under non-immersed (dry) conditions. However, the difference was more pronounced with warmer water (4 sub-

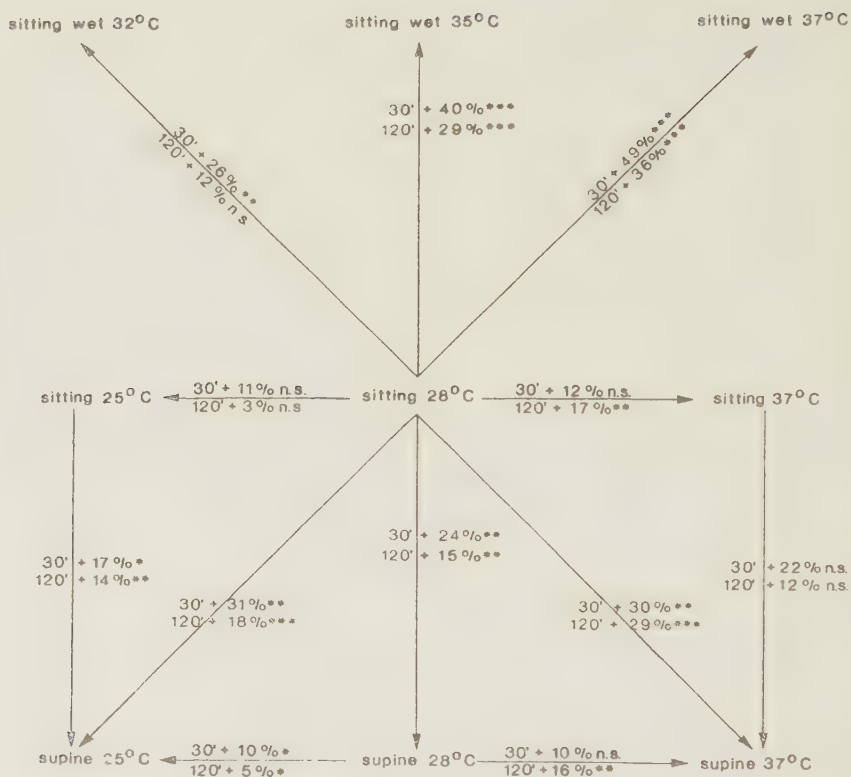


Fig 1. Mean relative differences in tissue nitrogen volumes eliminated after 30 min and 120 min. Results of immersion in water at 32°C, 35°C and 37°C, and of sitting and supine body position during dry conditions at 25°C, 28°C and 37°C are compared as indicated by arrows. Statistical calculations were made with paired comparisons and Student's t-test.

* $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.

jects, $n=8$). At the end of the 2 hr measurement period the nitrogen yield remained largest during immersion in warm water, but it also increased during immersion in neutral temperature water. In cool water, on the other hand, there was no significant difference compared to dry conditions (4 subjects, $n=8$). In Fig 2 the results presented in paper I are given as mean nitrogen elimination rates calculated per consecutive 30 min period. The calculations were based on determinations in subjects with normal body weights (3 subjects, $n=6$, at 32°C and 37°C ; 4 subjects, $n=8$, at 35°C . Cf paper I, Table I). The nitrogen elimination rate during the first 30 min period was significantly higher in all immersion experiments compared to non-immersion controls. The elimination rate was proportional to increasing water temperature. However, during the 30-60 min period only immersion in neutral or warm water caused a significant increase in the nitrogen elimination rate. In cool water the elimination rate was the same as during non-immersion. During the 60-90 and 90-120 min periods no statistically significant differences in nitrogen elimination rates were observed.

The nitrogen elimination rates for the different 30 min periods in subject L.N. who was 20 kg overweight (51) are given in Fig 3. A comparison with the results in the normal weight subjects presented in Fig 2 points to some fundamental differences. The overweight subject eliminated more nitrogen under all experimental conditions (cf I, Fig 3 and Table I). Furthermore, the difference in nitrogen elimination rate between the dry control situation at neutral temperature and immersion in cool water was more marked in the overweight subject. The differences in elimination rates between dry and wet conditions also seemed to persist in the 60-90 and 90-120 min periods. This is demonstrated by the diverging course of nitrogen elimination curves I, Fig 3, as opposed to the curves obtained in a normal weight subject which become more parallel after 60 min, I, Fig 2. Also in normal

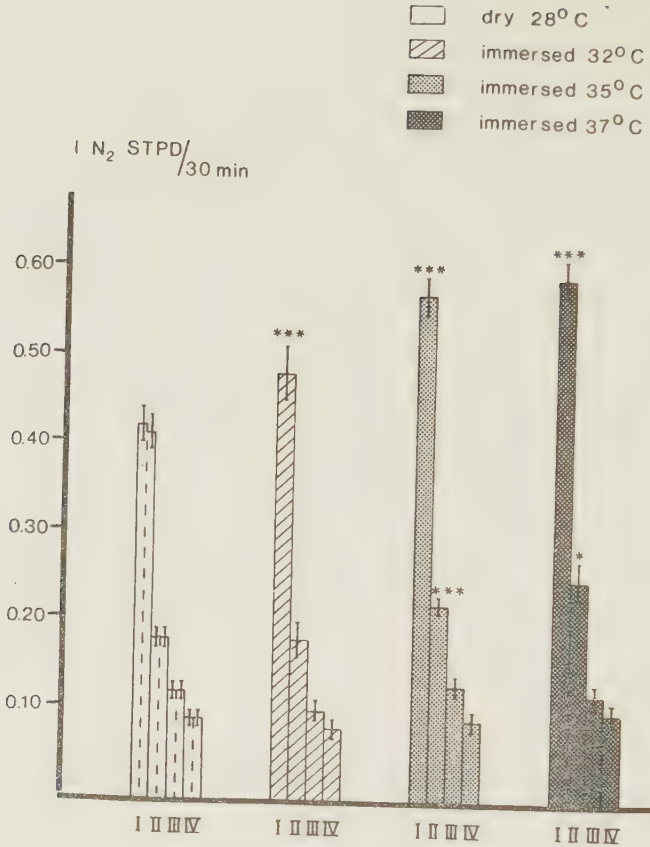


Fig 2. Mean nitrogen elimination rates and SEM in 1 N₂ STPD/30 min in normal weight sitting subjects during dry conditions at 28°C (split column: Results in 4 and 3 subjects, respectively, double determinations) and during immersion in water at 32°C (3 subj., double determ.), 35°C (4 subj., double determ.) and 37°C (3 subj., double determ.). Roman numerals refer to the following periods, I: 0-30 min, II: 31-60 min, III: 61-90 min, IV: 91-120 min. Results of reciprocal 30 min periods were compared referring to dry conditions as the control situation, using paired comparisons and Student's t-test. * $p < 0.05$, *** $p < 0.001$.

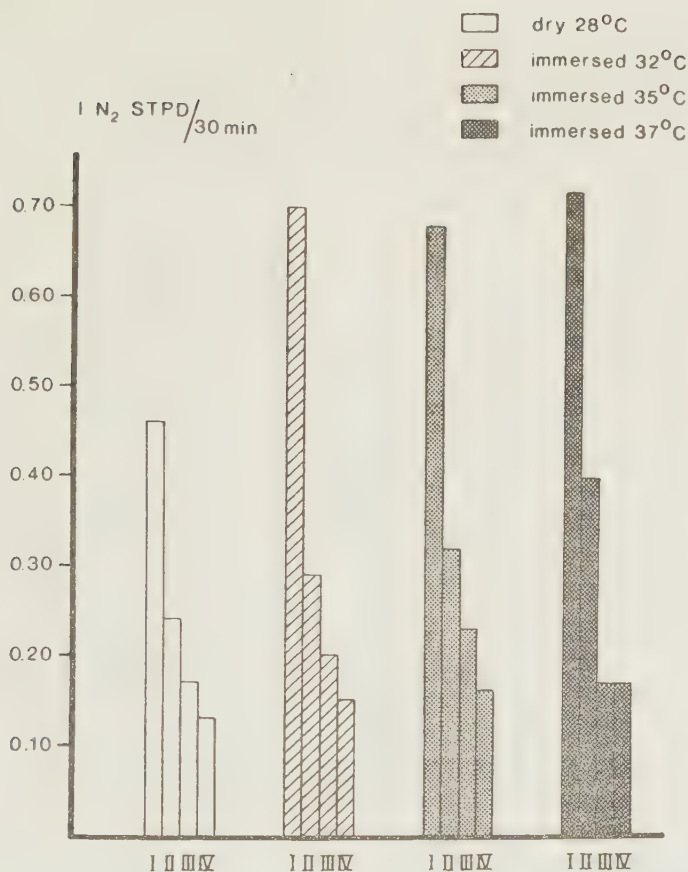


Fig 3. Mean of nitrogen elimination rates in $l N_2$ STPD/30 min in a sitting subject (double determinations) with about 20 kg overweight during dry conditions at 28°C and during immersion in water at 32°C, 35°C and 37°C. Roman numerals refer to the following periods, I: 0-30 min, II: 31-60 min, III: 61-90 min, IV: 91-120 min.

weight subjects slowly eliminating tissues appear to be influenced by immersion. Thus, mathematical fraction analysis of wash-out curves from experiments lasting 4 hr showed an expansion of the tissue fraction with a 10 min half-time from 300 to 500 ml of nitrogen apparently being derived from slower tissues (I).

Body position

The mean relative differences in nitrogen volumes obtained in sitting and supine body positions at ambient temperatures of 25°C, 28°C and 37°C (II) are indicated at the vertical arrows in the lower part of Fig 1. In the supine body position (6 subjects, n=12) there was a higher nitrogen yield compared to the sitting position throughout the 2 hr period in neutral temperature. This was also recorded in a cool environment (3 subjects, n=6). However, in the warm environment no statistically significant difference was observed. Fig 4 displays the mean nitrogen volumes eliminated during the different 30 min periods in supine and sitting body positions at 28°C (6 subjects, n=12). The elimination rate was significantly faster in the supine than in the sitting position during the first 30 min period, but there was no significant difference during the later phases.

Ambient temperature

The mean relative differences in nitrogen volumes obtained at the different ambient temperatures of 25°C, 28°C and 37°C in the sitting and supine body positions (II) are indicated by the horizontal arrows in the lower part of Fig 1. In a warm environment (37°C) there was a gradual increase with time in nitrogen elimination. During the first 30 min in sitting (4 subjects, n=8) and the first 60 min in the supine position (3 subjects, n=6) there were no significant differences in nitrogen yield when comparing warm to neutral temperature. However, in the later phases of the experiments significant differences developed (cf II, Table I) and persisted to the

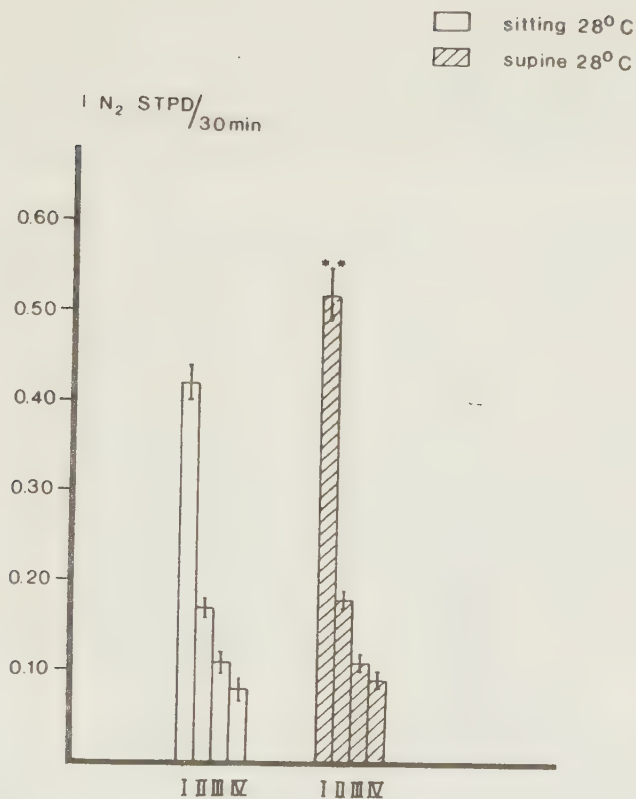


Fig 4. Mean of nitrogen elimination rates and SEM in $l N_2 \text{ STPD} / 30 \text{ min}$ in 6 subjects (double determinations) in sitting and supine body position (dry conditions at 28°C). Roman numerals refer to the following periods, I: 0-30 min, II: 31-60 min, III: 61-90 min, IV: 91-120 min. Results of reciprocal 30 min periods between sitting and supine body positions were compared using paired comparisons and Student's t-test. ** $p < 0.01$.

end of the 2 hr periods (Fig 1). This slowly developing increase in nitrogen elimination rate induced by the warm environment in sitting subjects is illustrated in Fig 5. Thus, in the first 30 min period the elimination rate was not statistically different from the neutral temperature, but in the following two periods there was a significant increase.

The cool environment (25°C) induced no change compared to a neutral temperature in the nitrogen yield and elimination rate in sitting subjects (4 subjects, $n=8$, Figs 1 and 5). There was, however, a slight increase in nitrogen volume in the supine position (3 subjects, $n=6$, Fig 1).

When comparing the nitrogen elimination in different ambient temperatures during immersion only minor or insignificant changes from neutral temperature (35°C) could be detected. However, when comparing sitting in cool (32°C) water with sitting in warm (37°C) water it was revealed that the latter condition caused a 20 % mean increase in eliminated nitrogen volume after 30 min and a 22 % mean increase after 120 min.

Effect of combined factors

The combined effect of supine body position and warm environment (3 subjects, $n=6$) seems to be additive in increasing nitrogen elimination (lower right quarter, Fig 1). Expressed in another way the most long lasting increase in nitrogen elimination rate compared to the control situation, sitting in neutral temperature, was obtained when combining the early effects of supine position with the later effects of warm environment (Fig 6). Compared to sitting dry in a neutral temperature, supine body position and cool environment resulted in a larger nitrogen volume (3 subjects, $n=6$) early in the experiments (lower left quarter, Fig 1). This difference was mainly due to a higher nitrogen elimination rate during the first 30 min (Fig 6) apparently induced by the supine body position (cf Fig 4).

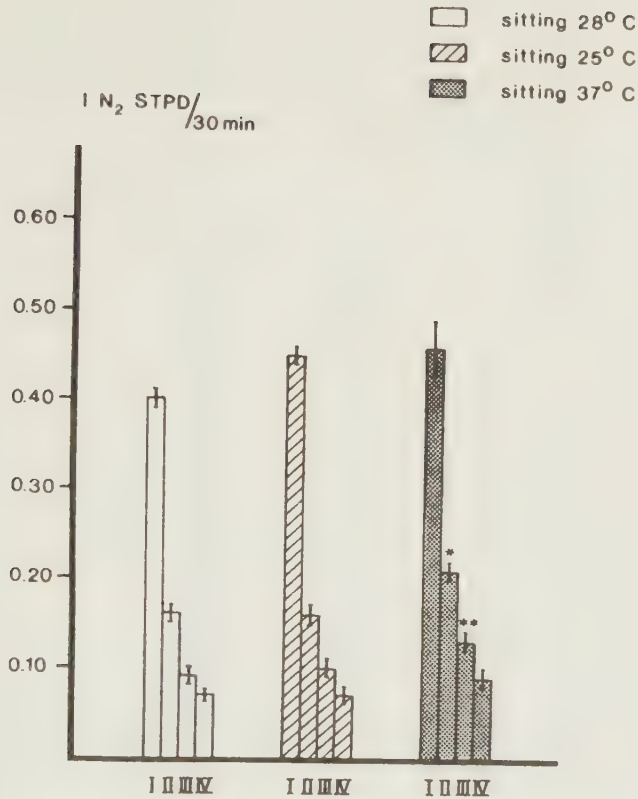


Fig 5. Mean of nitrogen elimination rates and SEM in $l N_2$ STPD/30 min in 4 subjects (double determinations) at ambient temperatures of 25°C, 28°C and 37°C (sitting body position in dry conditions). Roman numerals refer to the following periods, I: 0-30 min, II: 31-60 min, III: 61-90 min, IV: 91-120 min. Results of reciprocal 30 min periods in the different temperatures were compared referring to sitting at 28°C as the control situation, using paired comparisons and Student's t-test. * $p < 0.05$, ** $p < 0.01$.

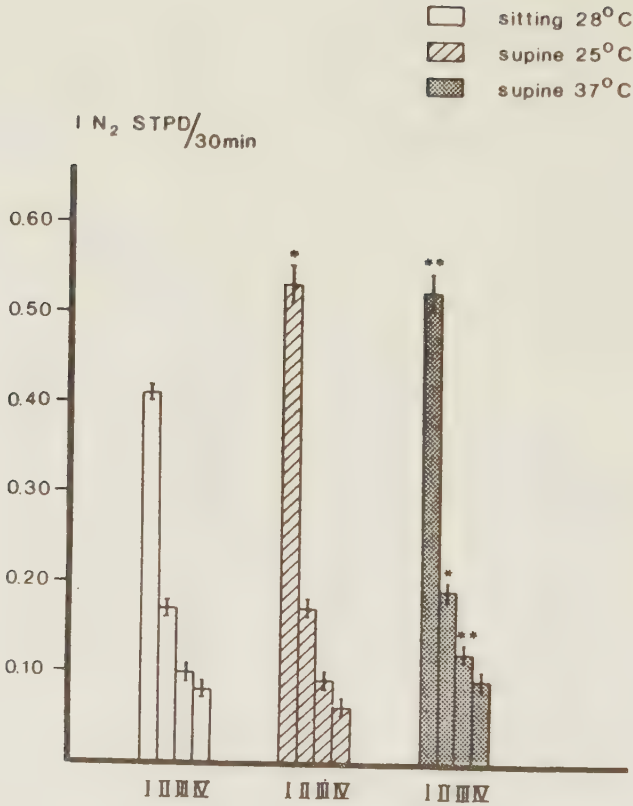


Fig 6. Mean of nitrogen elimination rates and SEM in l N₂ STPD/30 min in 3 subjects (double determinations) in sitting body position at 28°C and in supine body position at 25°C and 37°C (dry conditions). Roman numerals refer to the following periods, I: 0-30 min, II: 31-60 min, III: 61-90 min, IV: 91-120 min. Results of reciprocal 30 min periods in the different conditions were compared referring to sitting at 28°C as the control situation, using paired comparisons and Student's t-test. * p < 0.05, ** p < 0.01.

When measurements obtained in subjects sitting non-immersed in neutral temperature are used as a reference (center, Fig 1), it can be seen that the most efficient nitrogen elimination was obtained by immersion in warm (37°C) water (+ 49 % after 30 min; + 36 % after 120 min). Considerable enhancement of the nitrogen elimination was also observed during immersion in water of neutral (35°C) temperature (+ 40 % after 30 min; + 29 % after 120 min) and during supine body position in warm (37°C) environment (+ 30 % after 30 min; + 29 % after 120 min).

DISCUSSION

The present technique for measuring nitrogen elimination during non-immersed conditions yielded wash-out curves which agree well with those of Behnke, Thomson and Shaw (6) and Lundin (34). These authors also found that both the absolute nitrogen volumes and the course of the nitrogen elimination curves are influenced considerably by the size of the fat stores within the body because of the large nitrogen dissolving capacity of fat. This was confirmed in the present experiments by the increased nitrogen volumes and steeper elimination curves obtained in the subject who was 20 kg overweight as compared to the curves obtained in a normal weight subject. From the works of Behnke *et al* (6) and Lundin (34) it is evident that the nitrogen elimination pattern in the later parts of the present 2 hr experiment is mainly defined by the nitrogen release from body fat. Because the nitrogen elimination curves obtained in the overweight subject during immersion and dry conditions continued to diverge throughout the experiments it may be concluded that immersion did affect nitrogen release in fatty tissue. Furthermore, the mathematical fraction analysis of the nitrogen elimination curves in a normal weight subject indicated that part of the nitrogen from fatty tissue was eliminated rapidly enough during immersion to appear in a fraction with a 10 min half-time.

The fact that the effects of warming were more marked in the later parts of the present nitrogen elimination experiments offers some circumstantial evidence that nitrogen release from fatty tissue was influenced also by temperature.

In contrast to the prolonged effects which could be elicited with the present procedures, the augmentation of nitrogen elimination was shorter lasting with earlier tried procedures. With the method described by Margaria and Sendroy a 5 % admixture of carbon dioxide in the inhaled oxygen increased the eliminated nitrogen volume by 20 % during 30 min wash-out experiments (36). Moderate physical exercise has been shown by Behnke and Willmon to cause a 39 % increase in nitrogen elimination (8). This increase was mainly confined to the first 30 min of oxygen breathing. That physical exercise has only a relatively short lasting effect on nitrogen elimination is understandable, because the effect occurs in muscle tissue which even at rest has a rapid elimination rate with a half-time of 12-13 min (cf 34).

The increased rate of tissue nitrogen elimination induced by immersion and changes in body position presumably utilizes the same physiological mechanisms as do the changes in ^{133}Xe -non elimination from skeletal muscle under similar experimental conditions (IV). As elaborated on in Chapter II these changes may be ascribed to an increased cardiac output and local circulatory adjustments. Improved blood circulation may also explain the increased nitrogen elimination rate induced by a warm environment. In contrast, changes in pulmonary function, as discussed in Chapter II, are not important for the presently observed alterations in inert gas elimination.

In theory, changes in body temperature should influence nitrogen solubility in the tissues and hence influence nitrogen elimination rate. However, an increase in body temperature of 1°C would only decrease the solubility by about 1 % (25).

This would cause a 1 % increase in nitrogen partial pressure which would only cause an insignificant increase in nitrogen elimination from the tissues. Likewise, it may be calculated that the increase in the nitrogen diffusion coefficient that body temperature changes might induce is a negligible factor in explaining the present experimental results (25).

The possible influence on the present measurements by the elimination of free nitrogen in the gastro-intestinal tract deserve consideration. Theoretically, such changes in the immersion experiments may have been brought about by the hydrostatic pressure increasing the partial pressure of nitrogen in the gut. Furthermore, the enhancing effect on cardiac output by immersion and supine body position may possibly increase blood perfusion of the gastro-intestinal tract. However, the volume of free nitrogen in this region is probably not more than 150 ml and its normal elimination rate seems to be very slow (cf I). Therefore, a hydrostatically caused increase in nitrogen partial pressure in the gut which may amount to 5 % and even a 30 % increase in intestinal blood perfusion could not appreciably have contributed to the changes in tissue nitrogen elimination.

Experimental evidence has recently been presented by various authors indicating that there might be an appreciable endogenous nitrogen production in the human body (12,13,39). Studies by Cissik, Johnson and Rokosch attribute this nitrogen to alimentary sources (13). From their figures it appears that a high protein meal may result in nitrogen liberation via the lungs of between 100-150 ml per min. Fasting is stated to cause a slightly negative nitrogen balance. Even if these observations are correct they could not have relevance to the present results. The dietary regime in the present experiments was standardized (I,II) and would tend to give a neutral alimentary nitrogen balance in all the experiments and would therefore preclude any influence on the tissue nitrogen elimination measurements.

CHAPTER II

PHYSIOLOGICAL MECHANISMS CONTRIBUTING TO ENHANCED NITROGEN ELIMINATION

The rate of nitrogen elimination from the tissues is primarily a function of blood perfusion (cf 33: p.46). Hence, the slope of the whole-body exponential nitrogen elimination curve during oxygen breathing appears to be a function of cardiac output (6), and its distribution to peripheral tissue. Changes in blood flow consequently deserve consideration when discussing mechanisms by which various environmental factors may influence nitrogen elimination.

Earlier investigators have shown that cardiac output is larger in the supine than in the erect body position (10,35, 50) and also in warm environment (11,52). The circulatory changes related to immersion have however not been sufficiently explored before in human subjects. Earlier results were conflicting or based on too few experiments or obtained with unreliable methods. Thus, for instance, the studies made in the thirties by Kroetz and Wachter (30) and Gollwitzer-Meier (22) with the acetylene method indicate a change of between - 6 % and + 24 % in cardiac output during immersion in water of about 35°C compared to dry conditions. By contrast, Rennie, di Prampero and Cerretelli in 1968 (42) used a carbon dioxide rebreathing method and observed a 20-25 % reduction in cardiac output when their subjects were immersed in water of 34°C. These observations were not corroborated with our own preliminary results using a similar carbon dioxide technique which indicated a 32 % increase during immersion in water at 35°C (3).

The present studies were designed to give information of adjustments in central and peripheral circulation during immersion. For cardiac output measurements the more reliable dye

dilution technique was used (III). Furthermore, the pressures in the right atrium, pulmonary artery and brachial artery were recorded. In addition, the ^{133}Xe elimination technique was applied to investigate if possible changes in cardiac output corresponded to changes in blood flow in skeletal muscle during immersion and during different body positions (IV). Central hemodynamics during immersion were also evaluated by a study of regional lung function using radio-spirometry (V). This study served to confirm the theoretically founded view that disturbances in lung function cannot appreciably influence nitrogen elimination during immersion.

METHODOLOGICAL CONSIDERATIONS

Cardiac output was studied with dye dilution technique in 10 subjects during dry conditions and during immersion to the neck in water of neutral temperature (35°C) (III). Measurements of cardiac output, pulmonary and brachial arterial and right atrial pressures were made during air breathing and also during oxygen breathing, in order to simulate as closely as possible the special conditions of the present nitrogen elimination studies. Estimation of the increase of the central blood volume during immersion could also be made with the dye dilution technique. The same body container was used as in the nitrogen elimination studies described in Chapter I. The intra-vascular catheters were drawn through special fittings in the walls of the container. In order to minimize the infection hazard in the immersion experiments, the sites of catheter penetrations through the skin of the subjects' arms were covered with a sprayed-on watertight surgical dressing which provided good protection in all cases.

The transmural pressure of the heart is influenced by pleural pressure changes and these in turn are reflected by oesophageal pressure changes (17,38,45). Therefore the oesophageal pressure was measured during both dry and wet conditions. Be-

cause the presence of an oesophageal balloon is likely to disturb a subject and influence his blood circulation in various ways (32) oesophageal pressure was measured in separate immersion experiments.

The circulation in the anterior tibial muscle during immersion in water of neutral temperature (35°C , 12 subjects) and during the supine body position (6 subjects) was studied with the $^{133}\text{Xenon}$ elimination technique (IV). The disappearance of the inert gas $^{133}\text{Xenon}$ from a local deposit in the muscle could furthermore be expected to reflect nitrogen disappearance which is not easily directly studied (cf IV). In the $^{133}\text{Xenon}$ elimination studies immersion was made with water up to the level of the right atrium. In the so called dry conditions there was water up to a level 5 cm above the $^{133}\text{Xenon}$ injection site in order to provide similar local conditions in terms of temperature and moisture as in the immersion experiments proper. The measurements were made both during air and oxygen breathing. The studies of ^{133}Xe -non elimination from the anterior tibial muscle during supine and erect (65° angle to the horizontal plane) body positions were made with the subject lying passively on a tilting table.

Regional lung function was investigated in 7 subjects during dry and immersed conditions with $^{133}\text{Xenon}$ radiospirometry during both air and oxygen breathing (V). Four collimators outside the back of the body container recorded radioactivity in large apical and basal lung regions bilaterally. Lung perfusion was studied by recording the radioactivity after intravenous injection of $^{133}\text{Xenon}$ dissolved in saline. Ventilation was studied by recording changes in radioactivity in connection with inhalation of air or oxygen containing $^{133}\text{Xenon}$. Immersion may, by compressing the chest, disturb counting field geometry. This source of error was avoided by making all the recordings after inspiration to the maximal

inspiratory position. The experimental conditions were identical to those obtained during the cardiac output measurements where the subjects were immersed to the neck and neutral temperatures were employed in both the dry (28°C) and wet (35°C) experiments.

Treating the two lungs as an entity, regional lung perfusion was calculated from the count rate in apical and basal fields respectively, and expressed as percentages of the sum of the count rates in both fields. The calculations yielded an index of perfusion (ind. Q alv.) expressing the perfusion per alveolus. Regional lung ventilation was calculated as the percentage count rate in each region after inhalation of $^{133}\text{Xenon}$ divided by the percentage count rate in the same region after rebreathing. This gave an index of ventilation per alveolus (ind. V alv.). The ventilation-perfusion ratio (V/Q) was derived by dividing the ind. V alv. with the ind. Q alv.

RESULTS

Central hemodynamics during immersion

The cardiac output increased during immersion compared to dry conditions by a mean of 1.8 l/min (SD $\pm$ 1.1) or 32 % when air breathing and by a mean of 1.4 l/min (SD $\pm$ 1.2) or 26 % when oxygen breathing (III). The influence of immersion was in good agreement with the preliminary measurements with the CO_2 rebreathing method showing an average increase in cardiac output by 32 % (3). The increase in cardiac output was due to an increased stroke volume, since the heart rate was unchanged. The calculations of central blood volume in two subjects (four paired determinations in each) revealed a mean increase of 0.7 l (SD $\pm$ 0.5) as a result of immersion.

The right atrial pressure increased by a mean of 18 mm Hg (SD $\pm$ 7, air breathing) during immersion. In a separate ex-

perimental series the oesophageal pressure and hence the pleural pressure was found to increase by a mean of 5 mm Hg ($SD \pm 2$) during immersion (III). Compensating for this pressure change, the transmural pressure gradient of the right atrium could be calculated to be 13 mm Hg ($SD \pm 7$) higher on the average during immersion than during dry conditions. Calculating in the same way, the increase in the transmural pulmonary arterial pressure during immersion was on the average 12 mm Hg ($SD \pm 2$).

Peripheral hemodynamics during immersion and during supine body position

In the heart-catheterization studies a reduction in systemic vascular resistance of 30 % during air breathing and of 27 % during oxygen breathing was observed in immersed conditions compared to dry conditions (III). The left brachial arterial pressure was increased by a mean of about 10 mm Hg during immersion compared to dry conditions. This was about 5 mm Hg lower than the hydrostatic pressure increase induced by the external water column at the reference level of the pressure transducer. The transmural blood pressure in the brachial artery was thus calculated to have decreased about 5 mm Hg during immersion.

From the recordings of ^{133}Xe elimination in the anterior tibial muscle during immersion and the supine body position a rough estimate of muscle blood flow was obtained (IV). The blood flow increased from a mean of 1.8 ml/min $\times$ 100 g tissue during dry conditions to 4.1 ml/min $\times$ 100 g tissue ($+ 130\%$) during immersion to the heart level with air breathing. The increase was somewhat smaller during immersion with oxygen breathing ($+ 103\%$). The blood flow value during air breathing in the erect position was 1.1 ml/min $\times$ 100 g tissue compared to 2.2 ml/min $\times$ 100 g tissue ($+ 102\%$) in the supine body position.

Regional lung function during immersion

The perfusion per alveolus in dry conditions was low in the apical and high in the basal regions. With immersion the distribution of perfusion became more even. Thus, apical ind. Q alv. increased from 0.66 to 1.00 during air breathing and from 0.61 to 0.90 during oxygen breathing. The basal ind. Q alv. decreased from 1.27 to 0.98 during air breathing and from 1.31 to 1.11 during oxygen breathing.

The ventilation per alveolus was approximately uniform during dry conditions but increased in apical regions and decreased in basal regions during immersion. Thus, the apical ind. V alv. increased from 1.02 to 1.16 and the basal ind. V alv. decreased from 0.99 to 0.88 during air breathing. No change was seen during oxygen breathing.

The ventilation-perfusion ratio was high in the apical regions under dry conditions. Immersion caused a marked change towards a lower V/Q in the apical regions, from 1.56 to 1.17 during air breathing and from 1.72 to 1.24 during oxygen breathing. In the basal regions the V/Q increased from 0.78 to 0.90 during air breathing and from 0.75 to 0.84 during oxygen breathing.

DISCUSSION

The increase in cardiac output which was caused by the transition from dry to immersed conditions was due to an increased stroke volume. The increased stroke volume presumably was caused by the redistribution of blood into the thorax and an increased venous return. The increased central blood volume was also reflected by the transmural pressure increase in the right atrium. The resistance in the pulmonary circulation can be calculated to decrease during immersion. Consequently, the increase in pulmonary arterial transmural pressure may also be ascribed to the increase in central blood

volume. These changes in central blood circulation also involved the distribution of pulmonary perfusion. Thus, the greatly improved perfusion in apical lung regions during immersion may be attributed mainly to increased pulmonary blood flow and pressure.

As for changes in peripheral circulation during immersion the systemic vascular resistance decreased enough to allow for the increase in cardiac output without any major changes in arterial blood pressure. The reduction in vascular resistance might have been reflexly induced by the activation of various receptors for instance within the low pressure system. Thus, adjustments of the autonomic nervous control may occur by reduction in sympathetic and/or augmentation of vagal discharge (26,41). Decreased transmural pressure in the major systemic circulation caused by immersion might have further reduced the systemic vascular resistance due to partial elimination of the relatively high myogenic vascular tone that is present in dependent regions in the erect body position (cf IV,37).

With regard to the distribution of the increased cardiac output the measurements of ¹³³Xenon elimination in the anterior tibial muscle indicate a considerable increase in blood flow during immersion (IV). If it is assumed that a total skeletal muscle mass of 30 kg is involved in this reaction, the total increase in muscle blood flow would be about 690 ml/min during air breathing and 450 ml/min during oxygen breathing. The cardiac output increase being 1800 ml/min and 1400 ml/min, respectively, and allowing for the blood flow increase in muscle tissue, about 1000 ml/min remain for the increase of perfusion of other tissues both during air and oxygen breathing. Part of this increased flow appears to be directed to fat tissue. This is indicated by the mathematical fraction analysis of the long term nitrogen elimination studies in a normal weight subject as well as the obvious long standing increase in nitrogen elimination rate in the overweight sub-

ject during immersion (Fig 3).

The increase in nitrogen elimination during immersion can be fully explained by the improved blood circulation that occurs upon the transition from dry to wet conditions. As pointed out earlier, changes in nitrogen clearance from the tissues are largely blood flow dependent. A direct parallel in terms of the influence of blood flow on inert gas exchange is offered by the measurement of the local disappearance of ^{133}Xe -non in muscle tissue during immersion. The effects of immersion on the circulation are likely to be immediate and were indicated by a marked increase in the nitrogen elimination rate during the first 30 min of the nitrogen wash-out experiment (Fig 2).

The augmented nitrogen elimination in the supine compared to the sitting body position may be explained by circulatory changes brought about by similar mechanisms as during immersion. Thus, shifting from the erect position (on a tilting table) to the supine caused an increase in intrathoracic blood volume by about 500 ml (47). Studies of cardiac output changes indicate increases when the supine body position is assumed. However, the magnitude of the increases which may be derived from different publications vary between about 15-30 % (10,35,50), apparently because of discrepancies in experimental techniques. The rapid changes in ^{133}Xe elimination from a deposit in muscle tissue which were observed during shifts from erect to supine body position and vice versa (IV) are in accord with the effects observed early in the time course of the nitrogen elimination studies (Fig 4). The increases in total muscle blood flow which may be inferred from the ^{133}Xe elimination studies amounted to about 330 ml/min. Consequently, within the limits of possible increases in cardiac output there is also room for considerable increases in the perfusion of other tissues during the supine body position.

The effects of warming on nitrogen elimination were not striking during immersion, probably because immersion per se had such a dominating effect on circulation. In dry conditions, however, the warm environment clearly caused a higher nitrogen elimination rate than in neutral temperature (exemplified in Fig 5). This difference became evident in the 2nd and 3rd 30 min periods of the experiments. The time course of the temperature effects on nitrogen elimination appears to be due to the time required for the temperature load to evoke the circulatory changes that are dependent on the body temperature. These circulatory changes include an augmentation of cardiac output (11,52) and enhanced blood flow to the skin (43) and presumably also to the subcutaneous adipose tissue (cf II). In the present experiments under dry conditions the increase in ear temperature upon warming amounted to about 0.5°C after 2 hr. From the findings of Wetzler and Thauer (52) one may infer that this temperature change might induce a cardiac output increase of about 2 l/min. Such an increase in the nitrogen transport capacity of the circulation could well account for the observed enhancement of nitrogen elimination. As for the effects of increased temperature on cardiac output during immersed conditions no quantitative predictions can be made presently. Assuming a nitrogen elimination half-time for resting skeletal muscle tissue of about 12 min (34) and half-times for visceral tissues (except fatty tissues) to be even shorter (cf 28) these tissues would have a very low nitrogen content during the 2nd and 3rd 30 min periods. Hence, the nitrogen eliminated at increased rates in warm environment appear to have been derived from other sources, such as fatty tissue.

Cool as compared to neutral environment only influenced nitrogen elimination in the supine body position. There is no obvious explanation for the slightly larger nitrogen yield at the lower temperature. However, the possibility of unnoticed shivering or increased muscle tension cannot be completely

excluded.

The question may be raised if alterations in lung function accounted for some of the observed changes in nitrogen elimination. Theoretically, only a major deterioration in ventilation and perfusion of normal lungs could have any effect, and if so a negative one, on the exchange of nitrogen and other gases with low solubility in the blood (19). The present radiospirometric study actually demonstrated an improved regional ventilation-perfusion adaptation due to a more even distribution of perfusion (V). The possibility of major changes in ventilation-perfusion, with the character of diffuse or stratified inhomogeneity, appears to be ruled out by the observation by others of a reduction in arterial blood oxygen tension of only 10 mm Hg during immersion (15).

CHAPTER III

THE PREVENTIVE EFFECT OF DENITROGENATION DURING WARM WATER IMMERSION ON DECOMPRESSION SICKNESS IN MAN

Three factors have been demonstrated which act via physiological mechanisms to markedly increase tissue nitrogen elimination during oxygen breathing (I,II). These factors, immersion to the neck, assuming the supine body position and/or exposure to a warm environment all have this effect relative to sitting non-immersed in a neutral temperature.

The question arises as to whether these factors can be applied to influence the safety of decompressions in man. When planning the experiments it was realized that modified decompression procedures have usually required very large experimental series to be verified. Hence, it was decided to try a combination of the experimental factors, immersion and warming, which had been shown to have a maximal effect on nitrogen elimination.

Using ten volunteers a comparison was made of the frequency of decompression sickness after preoxygenation during immersion in warm water and after preoxygenation in dry conditions (VI).

METHODOLOGICAL CONSIDERATIONS

Preceded by a denitrogenation period, decompression sickness was provoked by decompressing the subjects in a pressure chamber to a subatmospheric pressure of 155 mm Hg which corresponds to an altitude of 38,000 feet. Oxygen breathing was continued during the observation time to prevent hypoxia. The reason for making decompression from an atmospheric pressure was that the symptoms of decompression sickness at simulated altitude are usually less severe and can more easily be cured

than the symptoms that appear upon diving. The denitrogenation period before decompression consisted of 25 min of oxygen breathing either during dry conditions or during immersion in warm water (37°C). The reason for limiting the pre-oxygenation period to 25 min was that in dry conditions it still permits a considerable chance for decompression sickness to occur within a 2 hr exposure at 155 mm Hg (cf III). A 25 min period is also sufficient to allow significant effects of warm water immersion on nitrogen elimination (cf Chapter I). During the observation period at 155 mm Hg the subjects performed a standardized leg exercise which is known to promote the appearance of symptoms of decompression sickness (16,21). When symptoms appeared or after an observation time of 2 hr, recompression began. In addition, the subjects were treated with hyperbaric oxygen as an extra safety measure. Three subjects were resistant to the ordinary provocation procedure and were given an extra tissue nitrogen load by 30 min air breathing at 2 ata before the denitrogenation period.

In designing these experiments a number of factors were taken into account which are known to introduce a risk of bias in decompression experiments of the present type. Such factors are unscheduled physical exercise, repeated pressure exposures within too narrow time intervals and the time of the day during the experiment (21). Furthermore, because there may be inter-individual differences in susceptibility to decompression sickness all subjects were tested both in dry and wet conditions.

Because the diagnosis of decompression sickness would depend on the subjects' own observations, these were recorded as reported by the subject without any leading questions. The subjects had not been informed in advance of the expected difference in the results of the two experimental series.

RESULTS

In all cases the symptoms of decompression sickness were joint pain or the so called bends. They usually started as a mild, ill-localized, dull discomfort in the vicinity of a joint. The bends were considered to be confirmed when the subject emphatically described well localized pain. Further confirmation of the diagnosis of decompression sickness was obtained in all cases by the disappearance of the symptoms during recompression.

In the 10 decompressions that were performed after denitrogenation in dry conditions 9 cases of bends were recorded. In contrast, the 10 decompressions after denitrogenation in warm water gave only 2 cases of bends. The difference in the proportions of bends in the two series of experiments was statistically significant; $p < 0.01$, Fisher's exact test (20).

DISCUSSION

Immersion in warm water during 25 min of oxygen breathing had a clear protective effect against decompression sickness compared to the same period of oxygen breathing during non-immersed conditions. It is highly likely that warm water immersion exerts this effect by decreasing nitrogen tension in bend sensitive tissues. Unfortunately, it is difficult to evaluate the quantitative changes in nitrogen tensions in different tissues. This is partly because the distribution of the total increase in blood flow accompanying immersion in warm water is not sufficiently known. However, in theory, the large increase in nitrogen elimination that occurs in the present experimental situation may be of benefit whether it is derived from tissues which in the control situation eliminate nitrogen more rapidly or more slowly. This view is supported by the observation in animal experiments that bends may arise

because of gas super-saturation in tissue fractions with widely differing nitrogen clearance rates (33).

As mentioned in the Introduction, physical exercise as well as carbon dioxide admixture to the inhaled gas also act by physiological mechanisms to increase tissue nitrogen elimination. Nevertheless, the risk of decompression sickness may be increased if these principles are applied during decompression as demonstrated by practical experience and experimental evidence (4,16,23,24,44). In contrast, the present method of denitrogenation during immersion in warm water distinctly lowered the incidence of altitude decompression sickness. There is good reason to assume that warm water immersion would be beneficial if utilized during decompression of divers and other compressed air workers.

In the present tests with a short lasting denitrogenation period the relative importance of immersion for promoting nitrogen clearance was obviously greater than that of warming (cf VI). However, in more long lasting decompressions the relative merit of placing the subject in a warm environment should increase. Furthermore, utilizing the supine body position instead of immersion appears more practical.

The present methods for making inert gas elimination more efficient may either be applied to shorten the duration of decompressions or to increase the safety of present decompression tables. The detailed quantitative aspects of such applications will require further studies. One further consequence of the present observations appears to be that more stringent standardization of the experimental procedures can be made, for instance, during testing of decompression tables. It should be emphasized that the increased blood circulation caused by immersion, assuming the supine body position, or warming may increase the uptake of inert gas during compression or at depth when the inert gas pressure in the alveolar

gas is higher than in the tissues. This would theoretically increase the risk of decompression sickness associated with the ascent.

When considering for diving safety the potential practical implications of immersion, body posture and environmental temperature it should be realized that all categories of personnel exposed to hyperbaric pressure may be subjected to variations in these factors. A diver may for instance return from the water to be decompressed in a dry decompression chamber. While in the water, the so called helmet diver is, from the hemodynamic point of view, not subjected to immersion if his suit is well inflated all the way down to the feet. The SCUBA* diver wearing a wet suit and taking the erect position is on the other hand subjected to maximal immersion effects when using a conventional breathing apparatus which delivers air at the same pressure as the water pressure at his mouth level.

* Self Contained Underwater Breathing Apparatus.

GENERAL SUMMARY

The risk of decompression sickness is an important problem during diving and compressed air work. It was decided to investigate if certain factors which are relevant to the special environment of diving and compressed air work might modify inert gas elimination and thus the risk of decompression sickness. These factors were immersion, body position and ambient temperature.

Tissue nitrogen elimination during 2 hr of oxygen breathing was studied in man using an electronic nitrogen meter and a closed circuit spirometer system. A container encasing the subject was employed to control the environmental conditions.

It was found that nitrogen elimination increased markedly during immersion in water to the neck compared to sitting dry in a neutral temperature (28°C). The increase was most pronounced in warm water (37°C), the difference in eliminated nitrogen volume amounting to 49 % after 30 min and 36 % after 120 min. The increase was more pronounced in water at neutral temperature (35°C) than in cool water (32°C). Nitrogen elimination during dry conditions was increased in the supine body position compared to sitting and in warm environment (37°C) compared to neutral (28°C). The increase in the supine body position was prompt while the increase in warm environment developed gradually throughout the experiment. Combining the supine body position with warm environment gave both a rapid and sustained increase in nitrogen elimination, the nitrogen volume exceeding that of the sitting position in neutral temperature by 30 % after 30 min and 29 % after 120 min.

In order to explain the increased nitrogen elimination rate during immersion, the hemodynamics of immersed subjects were studied. Cardiac output measured with the dye dilution technique was 26 % (oxygen breathing) to 32 % (air breathing)

larger during immersion in water at 35°C than in dry conditions at 28°C. This was due to a corresponding stroke volume increase based on a marked redistribution of blood into the thorax. These changes in central hemodynamics were reflected by a more even regional distribution of pulmonary blood perfusion during immersion as revealed by $^{133}\text{Xenon}$ radiospirometry studies. However, the more even ventilation-perfusion distribution in the lungs which was observed during immersion was insignificant for enhancing nitrogen elimination. Measurements of $^{133}\text{Xenon}$ clearance from a deposit in the anterior tibial muscle indicated that immersion more than doubled muscle blood flow, thus enhancing nitrogen elimination. In addition, it was suggested that a considerable proportion of the increase in cardiac output during immersion may be directed to other tissues such as fatty tissue. Therefore the large store of nitrogen retained in such tissue could be more rapidly mobilized.

The more rapid rate of tissue nitrogen elimination upon transition from sitting to a supine body position may be explained by the increase in cardiac output which is known to occur with alterations in body position. Support of the theory that tissue blood perfusion may increase was offered by the observation of a considerably more rapid $^{133}\text{Xenon}$ elimination in skeletal muscle tissue in the supine than in the erect body position.

The gradual increase in nitrogen elimination rate upon warming was considered compatible with the circulatory changes that are part of the thermoregulatory mechanisms of the body. It was then assumed that an increased blood flow to the skin would also engage the subcutaneous fat which in turn would aid in mobilizing its large nitrogen store.

A study was made to investigate if immersion in warm water could be used to influence the safety of decompression to

altitude in man. Denitrogenation by oxygen breathing for 25 min in water at 37°C or during dry conditions was followed by provocation of decompression sickness at an ambient pressure of 155 mm Hg. The occurrence of decompression sickness (bends) was 2 out of 10 cases after denitrogenation during immersion and 9 out of 10 cases after denitrogenation during dry conditions.

It is concluded that the circulatory effects of immersion, changes in body position and environmental temperature may be employed in order to influence the rate of tissue nitrogen exchange in a predictable way. Furthermore, it is concluded that immersion in warm water promotes the nitrogen clearance from bend sensitive tissues during oxygen breathing. It is considered highly likely that immersion, particularly in warm water as well as assuming the supine body position in a warm environment during decompression may reduce the risk of decompression sickness to divers and compressed air workers. It is further suggested that the present findings may be applicable for shortening decompression procedures. Because these findings also relate to the rate of nitrogen uptake, it is recommended that they should be taken into consideration when planning future pressure exposure experiments.

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